A.F. Shypko

Population-Based Estimation of the Prevalence of Dysplastic Dependent Pathology of Bronchopulmonary System among Children and the Risk of its Development Considering the Complex of Antenatal and Genealogical Factors

Kharkiv National Medical University, Ministry of Health of Ukraine, Kharkiv, Ukraine

Keywords:
social medicine; children's health; risk factors; bronchopulmonary system; prediction

Abstract.

Based on the study of the prevalence of potential genealogical and antenatal factors the most informative ones were determined. Their prognostic value was used as a criterion for assessing the risk of developing dysplastic dependent pathology of the bronchopulmonary system in children. Standardized pathometric tabular algorithm was developed using the Wald's sequential analysis modified by Hubler EV. An example of its application at the individual level was presented. The given algorithm was verified among children of both groups using the inverse method. The type I error rate (there was a high risk in the absence of pathology) was α=12.0%, and the type II error rate (there was a low risk in the presence of pathology) was β=9.8%. The specificity of the algorithm was 91.2% and its sensitivity was 88.0% that allows us to recommend it for using in the system of medical and social monitoring.

Problem statement and analysis of the recent research

Comprehensive consideration of potential risk factors for bronchopulmonary dysplasia (BPD) and dysplastic dependent pathology (DDP) of the bronchopulmonary system (BPS) in children to introduce standardized procedure for the prediction of these diseases is of great relevance to social medicine [1, 3-5]. The development and rapid flow of information on the pathogenic aspects of these diseases actualize the need to develop and improve the medical and organizational accompaniment as well as to adapt the existing models for providing medical care that from the standpoint of prevention approach can be implemented through the introduction of screening technologies and prediction algorithms [6, 9-11]. BPD is known to be a multifactorial disease with trigger and genetic factors including environmental ones [1, 3-5]. Damage to the respiratory tract in the neonatal period may affect lung ontogenesis and under certain conditions determine consequences of the disease [6, 7]. Therefore, the study of BPD in the continuing lung ontogenesis is important to prevent unfavorable outcomes, the development of DDP of the BPS in adulthood in particular [8, 9]. The question of predicting risk of BPD and DDP of the BPS considering antenatal and genealogical factors remains open [5, 6, 10, 11]. In this context, the development of standardized algorithm for assessing antenatal and genealogical factors is relevant.

The objective of the research was to provide evidence-based (clinical and statistical) justification of the risk assessment algorithm considering the complex of antenatal and genealogical factors being important for assessing children's health in dysplastic dependent pathology of the bronchopulmonary system.

Material and methods

The complex of antenatal and genealogical risk factors for BPD and DDP of the bronchopulmonary system was used. The study of their frequency in groups of children (252 persons with BPD and 252 persons without BPD) with further determination of the informative and prognostic values of each factor in relation to their use in the system of the population-based risk estimation was performed. Personalized analysis of the existing antenatal and genealogical factors in 116 children with BPD and 136 children with DDP of the BPS from two administrative regions of Ukraine (the first stratified population sample – SPS_1), 252 healthy children (the second stratified population sample – SPS_2) was made. When studying antenatal and genealogical factors specially prepared medical reports of expert evidence were used. Being completed for each patient they contained information on the presence of BPD or DDP of the BPS as well as information on the investigated factors obtained through interviews with parents using documented enclosed questionnaires completed by parents: the incidence of a complicated course of pregnancy (X_{31}); the age of the mother at the birth of her child (X_{32}); previous terminations of pregnancy in the mother (X_{33}); the presence of stigmata of dysembryogenesis in previous children (X_{34}); the presence of early and/or late gestosis during pregnancy (X_{35}); maternal smoking in the first trimester of pregnancy/the period of gestation (X_{36}); the presence of connective tissue disorders in the mother (X_{37}); the presence of chronic somatic diseases in the father (X_{38}); the presence of chronic somatic diseases in the mother (X_{39}); the presence of connective tissue disorders in the father (X_{40}); the presence of connective non-specific diseases in the mother (X_{41}); the presence of cardiovascular diseases in the mother (X_{42}), etc. The frequency, prognostic coefficient and informative value of certain factors were determined (using mathematical apparatus of variance analysis) for each investigated factor when making their comparative analysis in population-based samples of children from certain select areas of Dnipropetrovsk and Kharkiv regions. When making medical and statistical analysis (the one-way ANOVA) of factors frequency distribution of each factor gradation was used (Table 1). The informative values of factors (I, bit), their effect size (η2, %),

pathometric prognostic coefficients (PC_P) as well as the statistically significant difference in the average indicators were calculated using the Wald's sequential analysis modified by Hubler EV [2, 3].

Results and discussion

According to the results of comparative analysis of 20 antenatal and genealogical factors (Table 1 presents the most significant ones) 10 factors being the most informative were determined using standardized procedure. Their prognostic values were calculated [12]; standardized algorithm for predicting risk of DDP of the BPS in children was processed (Table 2).

Table 1

Genealogical and antenatal factors in children with dysplastic dependent pathology of the bronchopulmonary system

Code of factor	Medical and biological, phenotypic and genealogical factors			Population samples				PC, pat	I, bit	η^2, %
				n_1=252 SPS_1		n_{1-C}=252 SCP_2				
	Indicators		Gradations	abs.	P±m (%)	abs.	P±m (%)			
x_{31}	Complicated course of pregnancy		present	224	88.9±2.0	127	50.4±3.1	+2.4	0.474	17
			absent	28	11.1±2.0	125	49.6±3.1	-6.5	1.251	
	η^2=17.0	p<0.0001	total	252	100.0	252	100.0	-	1.725	
x_{32}	Age of the mother at the birth of her child		≤19	41	16.3±2.3	11	4.4±1.3	+5.7	0.340	9
			20-29	117	46.4±3.1	190	75.4±2.7	-2.1	0.305	
			30-39	85	33.7±3.0	49	19.4±2.5	+2.4	0.171	
			≥40	9	3.6±1.2	2	0.8±0.6	+6.5	0.091	
	η^2=9	p<0.0001	total	252	100.0	252	100.0	-	0.907	
x_{33}	Previous terminations of pregnancy		present	167	66.3±3.0	106	42.1±3.1	+2.0	0.239	6
			absent	85	33.7±3.0	146	57.9±3.1	-2.3	0.284	
	η^2=6.0	p<0.0001	total	252	100.0	252	100.0	-	0.523	
x_{34}	Stigmata of dysembryogenesis in children		present	59	24.3±2.7	19	7.5±1.7	+4.9	0.391	5
			absent	193	76.6±2.7	133	92.5±1.7	-0.8	0.065	
	η^2=5.0	p<0.0001	total	252	100.0	252	100.0	-	0.456	
x_{35}	Early or late gestosis		present	179	71.9±2.9	125	49.6±3.1	+1.6	0.167	5
			absent	73	29.0±2.9	127	50.4±3.1	-2.4	0.258	
	η^2=5.0	p<0.0001	total	252	100.0	252	100.0	-	0.425	
x_{36}	Maternal smoking in the first trimester of pregnancy		present	53	21.0±2.6	21	8.3±1.7	+4.0	0.255	3
			absent	199	79.0±2.6	131	91.7±1.7	-0.6	0.041	
	η^2=3.0	p<0.0001	total	252	100.0	252	100.0	-	0.296	
x_{37}	Connective tissue disorders in the mother		present	63	25.0±2.7	28	11.1±2.0	+3.5	0.245	3
			absent	189	75.0±2.7	224	88.9±2.0	-0.7	0.051	
	η^2=3.0	p<0.0001	total	252	100.0	252	100.0	-	0.296	
x_{38}			present	227	90.1±1.9	196	77.8±2.6	+0.6	0.039	3

	Chronic somatic diseases in the father		absent	25	9.9±1.9	56	22.2±2.6	-3.5	0.215	
	η^2=3.0	p=0.001	total	252	100.0	252	100.0	-	0.254	
X_{39}	Chronic somatic disease in the mother		present	204	81.8±2.5	172	68.3±2.9	+0.7	0.047	2
			absent	48	19.0±2.5	80	31.7±2.9	-2.3	0.141	
	η^2=2.0	p<0.001	total	252	100.0	252	100.0	-	0.188	
X_{40}	Connective tissue disorders in the father		present	75	29.8±2.9	42	16.7±2.3	+2.5	0.165	2
			absent	177	70.2±2.9	210	83.3±2.3	-0.7	0.049	
	η^2=2.0	p<0.001	total	252	100.0	252	100.0	-	0.214	
X_{41}	Connective non-specific diseases in the mother		present	47	18.7±2.5	21	8.3±1.7	+3.5	0.180	2
			absent	205	81.3±2.5	231	91.7±1.7	-0.5	0.027	
	η^2=2.0	p<0.001	total	252	100.0	252	100.0	-	0.207	
X_{42}	CVD in the mother		present	59	23.4±2.7	33	13.1±2.1	+2.5	0.130	2
			absent	193	76.6±2.7	219	86.9±2.1	-0.5	0.028	
	η^2=2.0	p<0.003	total	252	100.0	914	100.0	-	0.158	

Notes:

η^2 – effect size of the factor, %;

I – informative value of the factor, bit;

PC_p - pathometric prognostic coefficients of the factor, pat;

p – the level of statistical significance.

The algorithm was based on using prognostic values of the most informative factors and had a table equivalent containing the indicators of the assessment – prognostic coefficients (PC) and the rating scale as an outcome predictor. The algorithm involved independent signs of prediction only. When the strength of the correlation ($\pm r_{xy}$) between two factors was higher than ±0.70 one of the factors was excluded from the list of indicators. The use of tabular algorithm implemented pathometric approach to risk assessment. The principle of arriving at a predictive solution in pathometric algorithm (PA) reduced itself to the addition of prognostic coefficients following the sequence while analyzing the indicators. PA is known to consider the existing indicators as well as to minimize the number of steps which might be taken by prognostic technology due to the use of informative criteria (Table 1).

The following example shows the application of the algorithm: A 40-year-old Olga N. is pregnant (28 weeks of pregnancy). To predict the risk of developing dysplastic dependent pathology in her child considering the complex of antenatal and genealogical factors as well as the data of the primary healthcare records and standardized questionnaire completed by parents there has been revealed the following: there was a complicated course of previous pregnancy in her past medical history ($^{31}PC_P$=+2.4 pat); the age of the mother at the moment of her second child's birth will be 41 years ($^{32}PC_P$=+6.5 pat); there were previous terminations of pregnancy ($^{33}PC_P$=+2.0 pat); her first child suffers from stigmata (hyperelastosis cutis) of dysembryogenesis ($^{34}PC_P$=+4.9 pat). The procedure of prediction was stopped as predictive threshold was reached: PT= (+2.4)+(+6.5)+(+2.0)+(+4.9)=+15.8 pat, i.e. PT>15. Since the threshold predictive sum was reached we can predict with adequate reliability (in PC_{max} =+15 error does not exceed 5.0%) that there is a high

risk of developing dysplastic dependent pathology of the bronchopulmonary system in her second child

Table 2

Algorithm for predicting dysplastic dependent pathology of the bronchopulmonary system in a child considering the complex of antenatal and genealogical factors

Regional and environmental factors		Prognostic coefficients	
		Criterion	PC
1.	Complicated course of pregnancy in the past medical history	present	+2.4
		absent	-6.5
2.	Age of the mother at the moment of her child's birth	≤19	+5.7
		20-29	-2.1
		30-39	+2.4
		≥40	+6.5
3.	Previous terminations of pregnancy	present	+2.0
		absent	-2.3
4.	Stigmata of dysembryogenesis in the child	present	+4.9
		absent	-0.8
5.	Gestosis (early and/or late)	present	+1.6
		absent	-2.4
6.	Maternal smoking in the first trimester of pregnancy	present	+4.0
		absent	-0.6
7.	Dysplastic dependent pathology in the mother	present	+3.5
		absent	-0.7
8.	Chronic somatic diseases in the father	present	+0.6
		absent	-3.5
9.	Chronic somatic diseases in the mother	present	+0.7
		absent	-2.3
10.	Dysplastic dependent pathology in the father	present	+2.5
		absent	-0.7

Note: pathomeric coefficients are determined for each factor and then, systematically added; when the threshold sum (TS) of coefficients is reached (-13 or +13) the risk level is determined using the scale.

Rating scale for assessing the risk of dysplastic dependent pathology of the bronchopulmonary system		
$TS_{min} \leq -13.0$		$TS_{max} \geq +13.0$
minimal	uncertain risk	high risk

Fig. 1. Scale of personalized risk stratification for prevention of dysplastic dependent pathology of the bronchopulmonary system in children depending on the impact of antenatal and genealogical factors.

The given algorithm was verified among children of both groups (252 children with DDP and 252 children without DDP). The type I error rate (there was a high risk in the absence of

pathology) was α=12.0%, and the type II error rate (there was a low risk in the presence of pathology) was β=9.8%. Thus, the specificity of the algorithm is 91.2% and its sensitivity is 88.0% allowing us to recommend it for using in the system of medical and social monitoring.

Conclusions

1. Based on the study of the prevalence of 20 potential genealogical and antenatal factors the most informative ones were determined. Their prognostic value was used as a criterion for assessing the risk of developing DDP of the bronchopulmonary system in children.

2. Standardized pathometric tabular algorithm was developed using the Wald's sequential analysis modified by Hubler EV. An example of its application at the individual level was presented. The application of the given algorithm allows us to document the existent significant risk factors as well as to identify people at high risk of DDP of the bronchopulmonary system.

3. The given algorithm was verified among children of both groups using the inverse method. The type I error rate (there was a high risk in the absence of pathology) was α=12.0%, and the type II error rate (there was a low risk in the presence of pathology) was β=9.8%. The specificity of the algorithm was 91.2% and its sensitivity was 88.0% that allows us to recommend it for using in the system of medical and social monitoring.

Prospects for further research are determined by the need to develop the system of population-based and individual prediction of DDP of the bronchopulmonary system in the antenatal period as well as at the stages of postnatal ontogenesis considering other informative (medical and organizational, regional and environmental) factors.

References

1. Ahashkov VS, Klimenko TM. Bronchopulmonary dysplasia in newborns. Problemy suchasnoii nauky ta osvity. 2010;4:83-86.
2. Artamentova LA, Utelevskaia OM. Statistical methods in biology: manual for students of higher education institutions. Horlivka. Likhtar. 2008;248.
3. Hubler EV. Information science in pathology, clinical medicine and pediatrics. Leningrad. Meditsina. 1990;176.
4. Davidova IV. Development, clinical course and consequences of bronchopulmonary dysplasia in children [extended abstract of dissertation for Doctor of Medical Science]. Moscow. 2010;47.
5. Panchenko AS, Gaymolenko IN, Tikhonenko OA, et al. Bronchopulmonary dysplasia in children: clinic, diagnostics, consequences. Zabaykalskiy meditsinskiy vestnik. 2013;1:175-183.
6. Senatorova AS, Shypko AF, Lohvinova OL, Muratov HR. Optimization of medical care for children with bronchopulmonary dysplasia. Neonatolohiia, khirurhiia ta perynatalna medytsyna. 2014;IV;4(14):31-36.
7. Senatorova AS, Chaichenko TV, Shypko AF. Strategy of pediatric care reforming at the present stage. Neonatolohiia, khirurhiia ta perynatalna medytsyna. 2014;IV;3(13):15-19.
8. Snysar VI, Obolonskyi OI, Surkov DM. Bronchopulmonary dysplasia in preterm newborns: clinic, treatment and prevention (part 1). Zdorovye rebenka. 2013;4;47.
9. Frolova TV, Shypko AF, Okhapkina OV, Siniaieva IR, Stenkova NF. Health status in the child population of Kharkiv region. Pivdennoukraiinskyi medychnyi naukovyi zhurnal. 2014;9:86-90.

10. Shypko AF. Shypko AF. Actual issues of improving medical care for children with respiratory diseases. Medytsyna siohodni i zavtra. 2014;1(62):110-116.
11. Shypko AF. Problematic issues of resource maintenance of regional children's hospital and ways to improve health care for children. Eksperymentalna ta klinichna medytsyna. 2015;1(66):196-200.